U.S. Patent Application Serial No. 10/502,066 Amendment dated April 29, 2008 Reply to Office Action of October 29, 2007

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

(cancelled)

- 2. (currently amended) A method of reducing insulin resistance in a mammalian patient suffering therefrom comprising administering an effective amount of an acetylcholine esterase antagonist selected from the group consisting of donepezil, galanthamine, rivastigmine, tacrine, physostigmine, neostigmine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium, wherein the acetylcholine esterase antagonist is targeted to the liver.
- (original) The method of claim 2 wherein the insulin resistance is at least partially the
 result of inadequate levels of acetylcholine in the patient's hepatic parasympathetic nerve
 synapses.

4-8. (cancelled)

9. (currently amended) A pharmaceutical composition comprising a acetylcholine esterase antagonist selected from the group consisting of donepezil, galanthamine, rivastigmine, tacrine, physostigmine, neostigmine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium and at least one other drug used in the treatment of diabetes, and a pharmaceutically acceptable liver-targeting substance.

Conf. No. 8639

10-11. (cancelled)

- 12 (currently amended) The composition of claim 9 wherein the other drug comprises at least one of insulin, insulin analogues, sulfonvlurea agents, tolbutamide, acetohexamide, tolazamide, chiorpropamide, glyburide, glipizide, glimepiride, biguanide agents, metformin. alpha-glucosidase inhibitors, acarbose, miglitol, thiazolidinedione agents (insulin sensitizers), rosiglitazone, pioglitazone, troglitazone, meglitinide agents, repaglinide, phosphodiesterase inhibitors, anagrelide, tadalafil, dipyridamole, dyphylline, vardenafil, cilostazol, milrinone, theophylline, sildenafil, caffeine, cholinergic agonists, acetylcholine, methacholine, bethanechol, carbachol, pilocarpine hydrochloride, nitric oxide donors, products or processes to increase NO synthesis in the liver, 3-morpholinosydnonimine (SIN-1), molsidamine, nitrosylated N acetylevsteine, nitrosylated cysteine esters, nitrosylated L-2-oxothiazolidine-4-carboxolate (OTC), nitrosylated gamma glutamylcystein and its ethyl ester, nitrosylated glutathione ethyl ester, nitrosylated glutathione isopropyl ester, nitrosylated lipoic acid, nitrosylated cysteine, nitrosylated cystine, nitrosylated methionine, S-adenosylmethionine, products or processes to reduce the rate of NO degradation in the liver, products or processes to provide exogenous NO or an exogenous carrier or precursor which is taken up and releases NO in the liver, antioxidants. vitamin E, vitamin C, 3-morpholinosyndnonimine, glutathione increasing compounds, Nacetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxolate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, or and 5-adenosylmethionine.
- 13. (previously presented) The composition of claim 10 wherein the liver-targeting substance comprises at least one of albumin, bile salts and liposomes.

3

14. (currently amended) A kit comprising:

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an acetylcholine esterase antagonist selected from the group consisting of donepezil, galanthamine, rivastigme, tacrine, physostigmine, neostigmine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium, in a pharmaceutically acceptable carrier; and a pharmaceutically acceptable liver-targeting substance;

instructions for the administration of the acetylcholine esterase antagonist to reduce insulin resistance in a mammalian patient.

- 15. (original) The kit of claim 14 further comprising means to administer the acetylcholine esterase antagonist.
- 16. (cancelled)
- 17. (currently amended) A method of amplifying the effect of the hepatic parasympathetic reflex on skeletal muscle insulin sensitivity comprising administering an acetylcholine esterase antagonist selected from the group consisting of donepezil, galanthamine, rivastigmine, tacrine, physostigmine, neostigmine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium, wherein the acetylcholine esterase antagonist is targeted to the liver.
- 18. (currently amended) A method of increasing glucose uptake by skeletal muscle of a patient suffering from suboptimal hepatic regulation of blood glucose levels, comprising administering a acetylcholine esterase antagonist selected from the group consisting of donepezil, galanthamine, rivastigmine, tacrine, physostigmine, neostigmine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium, wherein the acetylcholine

U.S. Patent Application Serial No. 10/502,066 Amendment dated April 29, 2008 Reply to Office Action of October 29, 2007

esterase antagonist is targeted to the liver.

19. (currently amended) A method of reducing insulin resistance in a mammalian patient comprising administering a acetylcholine esterase antagonist selected from the group consisting of donepezil, galanthamine, rivastigmine, tacrine, physostigmine, neostigmine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, zanapezil, and ambenonium, wherein the acetylcholine esterase antagonist is targeted to the liver wherein said patient suffers from inadequate levels of acetylcholine in the hepatic parasympathetic nerve synapses.

20-21. (cancelled)

- 22. (currently amended) The method of claim 242 wherein the acetylcholine esterase is targeted to the liver using albumin.
- 23. (currently amended) The method of claim 212 wherein the acetylcholine esterase is targeted to the liver using a plurality of liposomes.
- 24. (currently amended) The method of claim 2+12 wherein the acetylcholine esterase is targeted to the liver using bile salts.
- (previously presented) The method of claim 2 wherein the acetylcholine esterase is administered by intravenous administration.
- (previously presented) The method of claim 2 wherein the acetylcholine esterase is

administered by transdermal administration.

- (previously presented) The method of claim 2 wherein the acetylcholine esterase is administered by oral administration.
- (previously presented) The method of claim 2 wherein the acetylcholine esterase is administered by intra peritoneal administration.
- 29. (previously presented) The method of claim 2 wherein the acetylcholine esterase antagonist is administered by portal vein injection.
- 30. (previously presented) The method of claim 2 wherein the acetylcholine esterase antagonist is administered by immobilization of the acetylcholine esterase antagonist on a solid support and implantation of the support adjacent the patients liver.
- 31. (previously presented) The method of claim 2 wherein the patient suffers from at least one of chronic liver disease, chronic hypertension, type II diabetes, fetal alcohol syndrome, gestational diabetes, age-related insulin resistance, and hepatic nerve damage.
- 32. (previously presented) The method of claim 5 wherein the patient is a human.
- (previously presented) The method of claim 2 wherein the insulin resistance is hepatic insulin sensitizing substance-dependent insulin resistance.

Conf. No. 8639

34-35. (cancelled)

36. (previously presented) The method of claim 2 wherein the patient suffers from suboptimal hepatic regulation of blood glucose levels.

37-45. (cancelled)